REMARKS/ARGUMENTS

I. PRELIMINARY REMARKS

The present application is directed to a method of using steroidal sapogenins and related compounds for treating cognitive dysfunction such as Alzheimer's disease.

By the Office Action dated April 4, 2003 all claims 1-32 are rejected.

Claims 13-30 are rejected as not being supported by the specification.

Claims 1-32 are rejected as being indefinite.

Claims 1-2, 9 and 32 are rejected as failing to properly recite a method or process.

Claims 1-2 and 9-32 are rejected for obviousness-type double patenting.

Claims 1-32 are rejected as anticipated, or alternatively rendered obvious, by the prior art.

By this Amendment claims 1-32 are canceled, and new claims 33-62 are presented. Applicants respectfully submit that by this amendment and the accompanying arguments and terminal disclaimer, all of the rejections have been overcome.

II. AMENDMENTS TO THE SPECIFICATION

The sentence, "The active agent or agents may, for example, be administered in a food product or beverage" has been added. The added sentence is supported in the specification at, for example, page 24, lines 24-26. Thus, the amendment to the specification adds no new subject matter to the application. In any event, it is well known that active agents can be administered through oral ingestion such as food or drink, so the amendment adds only information that would be obvious to those skilled in the relevant art based upon known methods of administering active agents to a subject.

The description of reference CN1096031A has also been amended to more accurately describe Applicants' understanding of this Chinese language reference. The amendment brings

The description of reference CN1096031A has also been amended to more accurately describe Applicants' understanding of this Chinese language reference. The amendment brings the description more closely in line with the description given on page 6, lines 90-14 of the specification. Inasmuch as the new description of the reference does not affect the breadth of the disclosure or claims of the application, and reflects the description previously in the specification, no new matter is added thereby.

III. CLAIM REJECTIONS

A. INITIAL COMMENTS

Claim 33 is based on original claim 10, with the sapogenins specified from those shown to be active in Tables 2 and 4.

Claim 34 is based on original claim 3, with the sapogenins specified from those shown to be active in Tables 2 and 4.

Claim 35 is based on original claim 1, with the sapogenin smilagenin specified.

Claims 36-57 are based on the specification at page 1, lines 4-23.

Claims 58 and 59 are based on original claims 1 and 2.

Claims 60 and 61 are based on original claim 31.

The recitation in the newly presented claims of treating various diseases is supported in the specification at page 1, lines 19-23. The recitation in claim 62 of oral ingestion is supported in the specification at page 24, lines 24-25.

B. REJECTION OF CLAIMS 13-30 AS UNSUPPORTED

Claims 13-30 are rejected under 35 U.S.C. § 112, second paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the

invention. In the Examiner's view, "The specification does not provide support for the treatment of a condition which is characterized by a deficiency in membrane-bound receptor number of [sic – or] function in a tissue, organ, cell type or organelle by modulation using any means."

Applicants do not understand the Examiner's position, and believes that the subject matter is fully supported. For example, the specification states on page 1:

> More particularly but not exclusively the invention is concerned with the treatment of conditions that are characterized by a deficiency in the number or function of membrane-bound receptors.

(page 1, lines 6-8). The specification further states on page 10:

> According to a ninth aspect of the present invention, there is provided a method for the treatment of a condition which is characterized by a deficiency in membrane-bound receptor number or function in a tissue, organ, cell type or organelle, the method comprising:
>
> modulating, directly or indirectly, the action of a cytosolic, nuclear or membrane-bound protein or receptor which, when it is activated by an agonist binding thereto, or when its activity is promoted by deactivation of an antagonist thereto, upregulates and/or normalizes the number and/or turnover of membrane-bound receptors in that tissue, organ, cell type or organelle.

(page 10, lines 19-28). The specification goes on to describe different embodiments and examples of this method. For example, 3 mg of sarsasapogenin per rat was fed to rats in their daily feed. (page 24, lines 24-25) This resulted in a significant increase in m_1 receptor mRNA in their brains as compared to the control group. (page 27, lines 11-14)

Accordingly, Applicants respectfully submit that the subject matter raised by the Examiner is supported in the specification. Applicants respectfully request that the rejection be withdrawn.

C. REJECTION OF CLAIMS 1-32 AS INDEFINITE

Claims 1-32 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Since all of the claims are now concretely defined in terms of disease states and active agents, the rejection under Section 112 has been overcome. Internal duplication of subject-matter has been removed, subject to the Applicants' need and right to claim the various aspects of the invention in the different ways necessary to provide effective coverage.

Claims 4 and 7. The Examiner contends that original claims 4 and 7 were substantial duplicates. Original claim 7 has no analog in currently presented claims 33-62. Accordingly, Applicants respectfully request that the rejection for substantial duplication is moot.

Claims 6 and 8. The Examiner contends that original claims 6 and 8 were substantial duplicates. Original claim 8 has no analog in currently presented claims 33-62. Accordingly, Applicants respectfully request that the rejection for substantial duplication is moot.

Claims 10-31. The Examiner contends that original claims 13-30 were "indefinite in that it is not clear who is being treated and how." (Office Action, page 2) The Examiner contends that original claims 10-31 were unclear in that "It is not clear from claims 10-31 if a human or an animal being treated is in need of such treatment." (Office Action, page 2)

Applicants do not understand the Examiner's position. If the Examiner was rejecting the claims for alternative claiming under MPEP 2173.05(h), then Applicants respond that the claims

as currently presented have been written to clearly avoid an alternative claiming rejection. Specifically, claim 1, from which all other claims depend either directly or indirectly, recites, "A method of enhancing cognitive function in an animal, including a human, which comprises . . . " The claim as written makes clear that the subject being treated is an animal, which encompasses either a human animal or a non-human animal. No ambiguity exists as to who or what is being treated.

The Examiner also states that, "It is not clear from claims 10-31 if a human or an animal is in need of such treatment." If the Examiner's position is that the claim is indefinite because it is not clear whether the subject is actually in need of treatment, then Applicants respond that the invention is one of enhancing cognitive function (which refers to functions such as thinking, reasoning, remembering, imagining and learning – see page 9, lines 26 to 27) using specific compounds. The invention is not limited to enhancing cognitive function in humans or in non-human animals that are "in need of" enhanced cognitive function. It is not clear that recipients of such a method could be easily categorized as being either "in need of " or "not in need of" such enhancement. The method would work even on perfectly mentally and physically healthy individuals, as well as those having specific disease states, for example those set out in the specification. In fact, any limitation which referred to someone being "in need of" enhanced cognitive function would inject uncertainty into the claim because it would be unclear what qualifies an animal or person as being "in need of" better thinking, reasoning, remembering, imagining, or learning capabilities. Even Applicants' undersigned representative has felt, at times, a strong desire if not outright need for enhanced cognitive function. Applicants accordingly submit that it would be unfairly limiting to require that the claims be limited to a method in which the recipient of the treatment "needs" enhanced cognitive function.

Claims 1-2, 9 and 32. The Examiner contends that original claims 1-2, 9 and 32 did not recite any steps involved in the method/process. The currently presented claims overcome the rejection by positively reciting one or more steps.

Requirement for Terminal Disclaimer. Claims 11-2 [sic – 1-2?] and 9-32 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,258,386 B1. In response, Applicants herein submit a terminal disclaimer thereby overcoming the rejection.

D. REJECTION OF CLAIMS AS ANTICIPATED AND/OR OBVIOUS

Claims 1-32 are rejected under 35 U.S.C. § 102(a) or (b) as anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over DE 4303214, Blunden et al, Ningyu et al "Sarsasapogenin Mechanism in Treating Senile Dementia," WO 99/16786 or Beiping Ma. The Office Action asserts broadly that each of those cited references "discloses saponin compounds and their user for the treatment of hosts. The claimed compositions and methods are anticipated therefrom [and] any differences [between the references and the present claims] would appear to be minor and nature and [therefore obvious]." Because the Office Action deals only very broadly with the claims versus the prior art Applicants will respond to the extent that they understand the Examiner's position.

The claims currently presented are directed to using smilagenin and/or anzurogenin-D. The structures of sarsasapogenin, smilagenin and anzurogenin-D are explained in the Table on page 7 of the specification. They are different compounds having different structures and, consequently, different properties.

Ningyu et al. discloses sarsasapogenin for treating senile demential. Ningyu does not teach or suggest any active agent other than sarsasapogenin as an agent for improving memory

and learning ability, and it would have been impossible without the benefit of hindsight for a non-inventive person of ordinary skill in the art to derive the invention as presently claimed from the Ningyu paper. The Examiner appears to assert that because smilagenin and anzurogenin-D are chemically similar in some ways to sarsasapogenin, the teaching of the use of one compound inherently anticipates or renders obvious the use of all possible compounds that can be said to be similar in some ways to the compound taught. Applicants respectfully disagree. Different compounds, though similar, can have vastly different pharmacological effects, so the teaching of a first compound hardly renders obvious the beneficial use of all possible related compounds.

The surprisingly beneficial activities of smilagenin and anzurogenin-D have been demonstrated in Tables 2 and 4 of the present application. The evidence of Table 2 shows smilagenin to have enhanced receptor activity in that test over sarsasapogenin by a large margin, which could not have been predicted. The evidence of Table 4 shows that smilagenin and anzurogenin-D had receptor expression activities in that test at 10 times lower concentration than sarsasapogenin, which could not have been predicted.

The activity of smilagenin or anzurogenin-D in overcoming cognitive dysfunction would have *not* been obvious from a knowledge that sarsasapogenin improves memory and learning ability. There was no way of predicting that any change to the sarsasapogenin molecule would be an improvement – it could equally have caused a reduction in activity (as shown by some of the compounds in Tables 2 and 4) or no change at all. Thus, in no way does Ningyu disclose or suggest the surprisingly beneficial results from administering "one or more active agents selected from the group consisting of smilagenin and anzurogenin-D" as claimed in claim 33.

The other cited art includes very large generic compound and/or disease definitions, with no clear pointer to the subject matter of the present claims. DE 4303214 A1, for example,

discusses the treatment of viral diseases generally with steroid saponins generally. The applicant goes on state that he is "convinced that a considerable portion of these diseases and illnesses of unknown or unclear original are caused by viruses . . . and that these diseases can be causally treated by means of the natural substances disclosed in his patent application." (page 9, lines 18-23) It is this rank speculation by the applicant that forms the basis for his further rank speculation that steroid saponins can be useful for treating almost every disease condition known to man, including: multiple sclerosis, scrapie, arthritis, autoimmune diseases, diabetes, and psoriasis (page 9, lines 4-15); asthma (page 16, line 10); HIV, hepatitis, polio, Ebola (page 15, 26, through page 16, line 2); cervical cancer, breast cancer, lung cancer, brain cancer, skin cancer, and prostate cancer (page 16, lines 15-24). This level of generality, in an attempt by the applicant to claim a broad family of compounds for treating virtually every disease that might conceivably have a viral origin, with no relevant showing of efficacy, renders this reference too general to enable and teach anything. Certainly, it no contains no appreciation of, or pointer towards, the surprisingly beneficial activity of the specifically claimed compounds of smilagenin and anzurogenin-D.

The other references cited are also too general to teach the surprising benefits of the specific compounds claimed. Any contention that the demonstrated level of activity of smilagenin or anzurogenin-D in enhancing cognitive function would have been obvious from a knowledge that sarsasapogenin improves memory, is hindsight reconstruction of that which only the present inventors have taught.

Applicants also wish to point out that an overlapping group of inventors has received U.S. Patent No. 6,258,386, directed to enhancing cognitive function using smilagenin. Since the structure of anzurogenin-D is further removed from sarsasapogenin than is the structure of

smilagenin, and since – as shown in Tables 2 and 4 – smilagenin and anzurogenin-D stand out amongst the other generally similar compounds as the only two where acceptable activity is preserved, the inventiveness of the claimed novel use of anzurogenin-D logically follows the inventiveness of similar use of smilagenin.

CONCLUSIONS

In view of the foregoing, it is respectively urged that all of the present claims of the application are patentable and in a condition for allowance. The undersigned attorney can be reached at 310-824-5555 to facilitate prosecution of this application, if necessary.

Respectfully submitted,

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